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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,703	06/27/2000	IAN ROSS DOYLE	13704/2	9876

26646 7590 07/03/2008

KENYON & KENYON LLP
ONE BROADWAY
NEW YORK, NY 10004

EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
07/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/486,703	DOYLE ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 1997*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3-2007; 11-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 11-5-97 has been entered.

Rejections Withdrawn

Claims 51-64 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Honda (Japanese Journal of Thoracic Diseases, 34 Suppl. Abstract only, December 1996; reference A11 on PTOL-1449 of 6-6-00 in view of Doyle et al (Advances in Critical Care Testing, Eds. Muller and McQueen, Springer-Verlag Telos, January 1997); reference A17 on the PTOL-1449 of 10-18-00) and Abe et al (Japanese Journal of Thoracic Diseases, 33(11):1219, Abstract only, November 1995; reference A10 on PTOL-1449 of 6-6-00) is withdrawn in view of the new rejection set forth below.

Claim Rejections - 35 USC § 102 and 103

Claims 51-64 stand rejected under 35 U.S.C. 102(b) as being anticipated by Doyle et al (Advances in Critical Care Testing, Eds. Muller and McQueen, Springer-Verlag Telos, January 1997; reference A17 on the PTOL-1449 of 10-18-00).

Doyle et al teach measuring SpA and SpB to screening for increases in a variety of patients including ventilated patients with no evidence of cardiorespiratory disease and screening for normal individuals (see page 152, Table 1) in sera (i.e. the instant blood) and the comparison of normal to other diseases. The "asymptomatic to lung damage or wherein

the clinical diagnosis of lung damage in the mammal cannot otherwise be confirmed without the aid of one or more invasive procedures" is seen to meet this limitation as instantly claimed because the ventilated patients had no evidence/symptoms of cardiorespiratory disease and is also evidence of disease and "during a period in which the onset of lung damage cannot otherwise be confirmed without the aid of one or more invasive procedures". Doyle et al teach that SP-B enters the circulation more readily than SP-A in a manner reflecting the severity of the lung injury (i.e. the instantly claimed lung damage). Doyle et al teach that when taken individually, daily changes in lung function were acutely reflected in concomitant variations in plasma SP-A, SP-B and SP-B/A. (see page 152, first full line of text). Further, the screening of "normal individuals" also meets the limitation of the claims, since these individuals would not be exhibiting a symptom specific to lung damage. The limitation of "predisposed to developing lung damage" is also met by the normal and ventilated patients because anyone alive is predisposed to developing lung damage from any of a number of causes (chemical insult, second hand smoke, pollution/ozone, trauma, etc) since they use their lungs while alive. Further, ventilated individuals are at risk from over-expansion lung injury or injury due to bacterial infection. As such, the patient populations tested by Doyle meet the limitations of the patient population claimed herein.

Applicants argue that there is a higher degree of inquiry by a physician for determination of asymptomatic versus normal. This is again not persuasive because in order to determine, normal or without disease as a medical basis for comparison one would have to rule out the same things as for the asymptomatic individuals. The specification does not set forth those criteria that applicants rely upon that distinguish normals from asymptomatic individuals. Applicants argue that even the definition requires the physician to consider the disease to which the patient is asymptomatic. The same would hold true for normals. In order to be classified "normal" with respect to lung injury or alveolar-capillary membrane damage the skilled artisan would have taken into account the disease

basis for comparison. As such, the degree of analysis of the population would be the same. A person who is used for a basis for comparison in a disease analysis of different patient populations has to have been assessed for the lung/alveolar capillary membrane damage, otherwise the person could not have been classified as "normal". This is the scientific method standard. One skilled in the art simply does not use people having the disease as "normals" in scientific study. Doyle et al compares OD (without evidence of cardiorespiratory disease) to normal levels. As such, they necessarily and inherently compared asymptomatic (i.e. without evidence of cardiorespiratory disease to normals). Applicants argue that the patient is asymptomatic to cardiorespiratory disease is irrelevant. This is not persuasive because Applicants specification and the art of record teaches that cardiorespiratory disease causes lung damage (i.e. the instant capillary-alveolar membrane damage) and lung damage is directly reflected by lung function. Therefore patient's without evidence of cardiorespiratory disease is highly relevant to the analysis. Applicants argue the definition of normal as "compared to what" ? and that the basis for comparison is the APE or ARDS patients and not free of cancer etc. This argument is again not persuasive because normal is free of lung injury for which the study was based. Applicants argue Remy-Jardin et al to illustrate how a smoking individual could be within the normal or OD groups of Doyle and still not be within the scope of the patient populations of the pending claims. This is not persuasive because the study of the art was respect to lung damage. The appropriate normal control was lung damage/injured lung as evidenced by the patient population without evidence of cardiorespiratory disease. Applicants essentially argue that normal values are patient population dependent and the basis for comparision must be so carefully defined that the normal population must be defined by the disease population and must be non-diseased with respect to that specific population and the skilled artisan would expect this as the basis and that populations can be mixed. This rationale casts doubt on the validity of Applicants own studies, studies that have not been so rigorously controlled and use the same "normal". The skilled artisan

would view normal as the study comparison. The study of Doyle et al looked at injured lung. Therefore normal would be viewed by the skilled artisan as non-injured lung (i.e. the population of no evidence of cardiorespiratory disease). Applicants argue that no evidence of cardiorespiratory disease is not equivalent to no evidence of lung damage or asymptomatic and that the patient populations are necessarily different. This is not persuasive, the patient populations are not necessarily different and necessarily overlap. As such, Doyle et al anticipates the instantly claimed invention. Applicants argue the fact senario in Eli Lilly v Teva 2004 U.S. District LEXIS 14724, where administration to a genus did not anticipate a species. In the instant case, we do not have a species within a genus of diseases/disorders. In the instant case there was "no evidence of cardiorespiratory disease", this would have meant to the skilled artisan that these patients were examined for markers and symptoms of cardiorespiratory disease which includes lung injury. Applicants' theoretical arguments are not persuasive and Doyle et al inherently anticipates the instantly claimed invention.

Claims 51-72 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Doyle et al Am. J. Respir. Crit. Card. Med. 1994l 149;A576; of record hereinafter Doyle A.) in view of Doyle et al (Advances in Critical Care Testing, Eds. Muller and McQueen, Springer-Verlag Telos, January 1997; of record hereinafter Doyle B), Doyle et al (Am. J. Respir. Crit. Care. Med. 152:307-317, 1995; of record hereinafter Doyle C), Honda (Japanese Journal of Thoracic Diseases, 34 Suppl. Abstract only, December 1996; of record) and Abe et al (Japanese Journal of Thoracic Diseases, 33(11):1219, Abstract only, November 1995; of record).

The claims are drawn to screening asymptomatic patients for lung injury or alveolar-capillary damage comprising screening for an increase in the level of SP-B in a body fluid in an asymptomatic patient as compared to a normal reference level.

Doyle A teaches surfactant proteins in the plasma of patients with respiratory disease. Doyle A teaches the levels of SP-A and SP-B in normal individuals, those with no evidence of cardiorespiratory disease, adult respiratory distress syndrome and actue cardiogenic pulmonary edema. Doyle A teach that SP-A and SP-B enter the circulation during lung injury and SP-B enters more readily and may provide a better indicator of lung trauma.

Doyle B teaches that SP-B enters the circulation more readily than SP-A in a manner reflecting the severity of the lung injury (i.e. the instantly claimed lung/alveolar-capillary membrane). Doyle et al teach that when taken individually, daily changes in lung function were acutely reflected in concomitant variations in plasma SP-A, SP-B and SP-B/A. (see page 152, first full line of text).

Doyle C teaches that serum SP-A is an acute indicator of lung function and alveolo-capillary membrane injury.

Honda teach the measurement of surfactant proteins A and D in the sera of patients with idiopathic interstitial pneumonia (IIP) by enzyme-linked immunosorbent assay using monoclonal antibodies against humans SP-D and SP-A as compared to healthy volunteers (i.e. the instant normal). Honda teaches that the results suggest that SP-D and SP-A, can enter the blood stream easily due to injury at the alveolar-capillary membrane. Further, the serum SP-D and SP-A concentrations appeared to reflect disease activity (see abstract) and could be used to diagnose IIP.

Abe et al teach that the serum levels of SP-A in patients with IIP and that the SP-A levels correlated closely with the clinical course and rose significantly during exacerbations of IPP (see abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time that the invention was made to diagnose lung injury or alveolo-capillary membrane injury at the earliest time by diagnosing asymptomatic patients for increases in lung damage and damage at the alveolar-capillary membrane by assaying for an increase in the

SP-B of Doyle A because Doyle B teach that SP-B enters the circulation more readily than SP-A and Doyle B and C teach that SP-A reflects the severity of the lung injury and damage at the alveolo-capillary membrane and Abe and Honda teach that surfactant levels correlates closely with lung disease exacerbations and it is immediately apparent that the SP-B levels can be used to measure/monitor disease onset or activity in asymptomatic individuals because the levels of SP-B reflect severity of lung injury/alveolo-capillary membrane damage. As such, one skilled in the art would be able to reasonably able diagnose asymptomatic patients for lung injury, damage at the alveolar-capillary membrane, diagnose IIP or monitor lung disease activity in IIP patients by screening for increases in SP-B as compared to normal because one skilled in the art would readily expect that SP-B in the serum/plasma would increase early because Doyle A and B teach that SP-B enters the circulation more readily than SP-A and Honda teaches that both SP-A and SP-D levels are increased and Abe et al teach that SP-A levels closely correlate with disease and therefore lung injury and damage at the alveolar-capillary membrane.

Status of the Claims

Claims 51-72 stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor Shanon Foley can be reached on 571-272-0898.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia A. Duffy/

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645